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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/715,556	11/19/2003	Swen Holder	03806.0590-00	5066

22852 7590 02/01/2007  
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EXAMINER
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HABTE, KAHSAY

ART UNIT	PAPER NUMBER
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1624

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/01/2007	PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

**Office Action Summary**

Application No.

10/715,556

Applicant(s)

HOLDER ET AL.

Examiner

Kahsay Habte

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 11 January 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-16, 29 and 30 is/are pending in the application. (claim renumbered)
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 29 is/are allowed.
- 6) ☒ Claim(s) 1-16 and 30 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

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### **DETAILED ACTION**

1. Claims 1-16 and 29-30 are pending in this application.

Not that the original claims were 1-28. Applicants have deleted claims 17-25 and added new claims 26-27. The new added claims are renumbered as 29-30.

It is unclear the status of original claims 26-28.

### ***Continued Examination Under 37 CFR 1.114***

2. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 1/12/2007 has been entered.

### ***Claim Rejections - 35 USC § 112***

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-16 and 30 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed,

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had possession of the claimed invention. In claim 1, the new proviso "wherein when Ar is a 9-membered bicyclic heterocycle containing one or more heteroatoms selected from N, O and S, Ar is unsubstituted" is a new matter. The concept of linking the substitution of Ar to the definition of Ar = 9-membered bicyclic heterocycle containing one or more heteroatoms selected from N, O and S, is a new concept.

Applicants indicate there is support in the specification at pages 3-4 for said proviso, but there is no written description for the phrase "wherein when Ar is a 9-membered bicyclic heterocycle containing one or more heteroatoms selected from N, O and S, Ar is unsubstituted".

### ***Claim Rejections - 35 USC § 102***

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

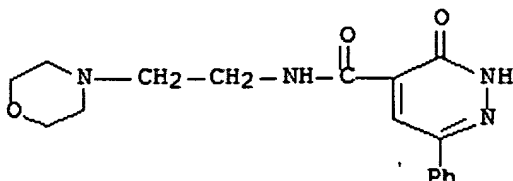
Claims 1-6 are rejected under 35 U.S.C. 102(a) as being anticipated by Nagato et al. WO 2002022587 A1. Cited reference teaches one compound of interest: 2,3-dihydro-N-[2-(4-morpholinyl)ethyl]-3-oxo-6-phenyl-4-Pyridazinecarboxamide that is the same as applicants compound when applicant's formula (I) has the following substituents:

A = CONH-CH<sub>2</sub>-CH<sub>2</sub>-morpholinyl (i.e. A = heterocyclyl-CH<sub>2</sub>-CH<sub>2</sub>-) and Ar = phenyl. See below.

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RN 404933-57-9 CAPLUS

CN 4-Pyridazinecarboxamide, 2,3-dihydro-N-[2-(4-morpholinyl)ethyl]-3-oxo-6-phenyl- (9CI) (CA INDEX NAME)



Applicants can overcome this rejection by providing an English translation of the foreign priority document.

### ***Claim Rejections - 35 USC § 103***

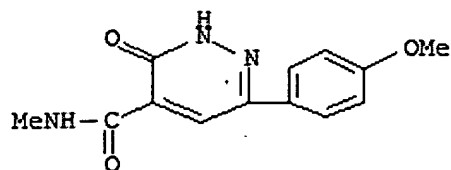
5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yoshizaki et al. (WO 99/44995). Cited reference discloses a compound of interest: 2,3-dihydro-6-(4-methoxyphenyl)-N-methyl-3-oxo-4-Pyridazinecarboxamide that is almost the same as applicants when applicant's formula (I) has the following substituents:  
Ar = phenyl substituted with methoxy; A = CONH-methyl (see below).

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RN 243862-95-5 CAPLUS

CN 4-Pyridazinecarboxamide, 2,3-dihydro-6-(4-methoxyphenyl)-N-methyl-3-oxo-  
(9CI) (CA INDEX NAME)

The only difference between applicant's compound and the prior art compound is the presence or absence of a methyl group on the phenyl ring. Applicant's compound is substituted by -OH on the phenyl group and the prior art compound is substituted by methoxy on the phenyl group. Compounds that differ only by the presence or absence of an extra methyl group or two are homologues. Homologues are of such close structural similarity that the disclosure of a compound renders *prima facie* obvious its homologue. The homologue is expected to be preparable by the same method and to have generally the same properties. This expectation is then deemed the motivation for preparing homologues. Of course, these presumptions are rebuttable by the showing of unexpected effects, but initially, the homologues are obvious even in the absence of a specific teaching to add or remove methyl groups. See *In re Wood*, 199 USPQ 137; *In re Hoke*, 195 USPQ 148; *In re Lohr*, 137 USPQ 548; *In re Magerlein*, 202 USPQ 473; *In re Wiechert*, 152 USPQ 249; *Ex parte Henkel*, 130 USPQ 474; *In re Fauque*, 121 USPQ 425; *In re Druey*, 138 USPQ 39. In all of these cases, the close structural similarity between two compounds differing by one or two methyl groups was itself sufficient show obviousness. See also MPEP 2144.09, second paragraph.

***Claim Rejections - 35 USC § 112***

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 9-16 and 30 (numbered as claim 27) are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. In claims 9 and 16, it is recited a method of inhibiting CDK2 *in vivo*, but the specification is not enabled for such a scope.

A number of factors are relevant to whether undue experimentation would be required to practice the claimed invention, including "(1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims." In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

(1). Breadth of Claims: Claims 9-16 are directed to a method for inhibiting CDK2 *in vivo* that comprises administering a physiologically active amount of a compound of formula (I) to a patient in need thereof.

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a. Scope of use - The scope of use that applicants intend to claim is very broad.

The instant claims 9 and 16 appear to be reach through claim. Reach through claims, in general have a format drawn to mechanistic, receptor binding or enzymatic functionality and thereby reach through any or all disease, disorders or conditions, for which they lack written description and enabling disclosure in the specification thereby requiring undue experimentation for one skill in the art to practice the invention. Note that a method inhibiting CDK2 *in vivo* is not different from the claim language "A method of inhibiting CDK2 in a patient". The claim covers the treatment of any disease that involves inhibition of CDK2. This could cover any person healthy or sick.

b. Scope of Compounds - The scope of the compounds is also broad. It is apparent that hundreds of millions of combinations of compounds can be created from the definitions, owing especially to broad scope of A, A1, A2, R, R1 and R2.

(2). Direction of Guidance: Applicants indicate that their compounds can be used for the inhibition of the kinase CDK2 and also disclose that CDK2 is usually part of a complex, such as CDK2/cyclin A or CDK2/cyclin E complexes. The amount of direction or guidance is minimal.



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(3). State of Prior Art: There is no evidence of record that compounds structurally similar to these pyridazinone derivative compounds of formula (I) or indeed are in use *in vivo* for the treatment of myriad disorders.

(4). Working Examples: Test procedures and assays are provided in the specification at page 110 only for 37 compounds and it is concluded that the representative compounds of formula (I) demonstrated positive inhibitory activity with  $IC_{50}$  ranging from 0.012  $\mu$ M to 0.905  $\mu$ M, however, there is nothing in the disclosure regarding how this *in vitro* data correlates to the treatment of myriad disorders.

(5). Nature of the Invention and Predictability: The invention is directed to inhibiting cancer cells in general. It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved," and physiological activity is generally considered to be an unpredictable factor. See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). There is no reasonable basis for assuming that the myriad of compounds embraced by the claims will all share the same physiological properties since they are so structurally dissimilar as to be chemically non-equivalent and there is no basis in the prior art for assuming the same. Note *In re Surrey*, 151 USPQ 724 regarding sufficiency of disclosure for a Markush group.

(6). The Quantity of Experimentation Necessary: Immense.

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(7). The Relative Skill of Those in the Art: The relative skill is extremely very low.

It is recommended that applicants amend the claim as "A method of inhibiting CDK2 activity *in vitro*" to overcome this rejection.

### ***Allowable Subject Matter***

7. Claim 29 (numbered as claim 26) is allowed.

### **Conclusion**

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kahsay Habte whose telephone number is (571) 272-0667. The examiner can normally be reached on M-F (9.00AM- 5:30PM).

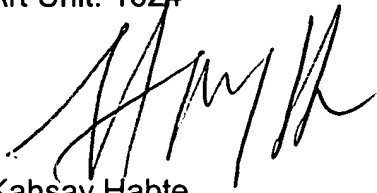
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached at (571) 272-0661. The fax phone number for the organization where this application or proceeding is assigned is (571)-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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A handwritten signature in black ink, appearing to read 'Kahsay Habte', written over the printed name.

Kahsay Habte  
Primary Examiner  
Art Unit 1624

January 29, 2007